Quick guide

Nitric oxide

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Not to be confused with… Nitrous oxide (N_2O), a.k.a. laughing gas. But although nitric oxide (NO) might not make you giggle, this news-making molecule does just about everything else.

What is it? NO is an intercellular messenger with multiple physiological functions. It was the first gas found to act as a signalling molecule in animals and continues to lead the field over its upstart rival, carbon monoxide.

It first came to prominence… In the early 1980s. Until then, NO was only a poisonous air pollutant as far as most people were concerned. Then scientists identified NO as the mystery endothelial-derived factor that relaxes blood vessels. Any who were initially incredulous were soon trampled by the mob boarding the NO bandwagon.

What does it do? What doesn't it do is the better question — *Science* didn't name NO 'Molecule of the Year' in 1992 for nothing. For physiologists, NO entered the arena as a signal that dilates blood vessels; NO is released by endothelial cells lining the vessels and has a critical role in maintaining blood pressure. Since then, scientists have found that NO acts in the immune system to kill 'foreign bodies', such as bacteria and tumor cells, and in the brain to increase neurotransmission and perhaps play a role in learning and memory. NO also triggers penile erection during sexual excitement and participates in peristalsis of the gut.

Other speculated functions include… Recently, NO has also been implicated in olfactory memory, the control of cell proliferation during development and circadian rhythms.

How does it work? Cells make NO from the amino acid L-arginine, with an enzyme called nitric oxide synthase (NOS). Isoforms of this enzyme include neuronal NOS, endothelial NOS and inducible NOS, which is present in macrophages, among other cells. Once produced, NO can diffuse right through cell membranes (being a gas) but has a limited lifespan (being a highly reactive gas).

Who are its known associates? The main effector of NO is the guanylate cyclase enzyme; NO stimulates guanylate cyclase to produce cGMP, which in turn mediates many of nitric oxide's physiological functions.

What happens without it? It's a well-known fact that lack of NO causes most human ills. In studies with varying degrees of credibility, scientists have found that diminished nitric oxide (known as "no-NO") causes pulmonary hypertension, impotence, urinary voiding disorders, male aggression — even criminal aggression — and hair loss.

It's been completely rehabilitated, then? NO has come a long way from its original toxic reputation but the news isn't all good. Even as a messenger, NO can cause damage; it's been implicated in neurodegeneration, can trigger inflammatory diseases, and excessive release in response to infections can lead to dangerously low blood pressure, or septic shock.

So is NO news good news? It certainly is for Louis Ignarro, Ferid Murad, and Robert Furchgott, who won last year's Nobel Prize for Physiology or Medicine for identifying NO as a biological messenger molecule. But NO research is also reputed to have changed the lives of countless other men (and women), because the discovery of nitric oxide's many physiological roles helped lead to the development of the anti-impotence drug Viagra.

Most likely to be mentioned by… Ignarro, Murad, Furchgott, Salvador Moncada (who many felt should have shared the Nobel prize with them), John Garthwaite and Solomon Snyder … to name but a few.

So is there a mountain of publications on NO? A small hill, certainly. In the past three years there have been 13,588 papers that focus on NO, according to Medline.

Does it have commercial potential? You bet. A search of recent patents filed with the US Patent Office reveals hundreds of NO-based inventions for biomedical applications. Viagra aside, scientists are using nitric oxide's powers of vasodilation to treat conditions such as hypoxic respiratory failure in newborn babies and cardiovascular fibrosis.

Where can I find out more?

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